REMARKS

Upon entry of the amendments made herein, claims 1-45 are pending in this application. Claims 1, 3, 5-11, 14-16, 18, 20, 30-32, 34, 36, and 37 have been amended to further define the invention. Specifically, Applicants have removed original steps i-iii from claim 1 and renumbered each of the original steps iv-vii respectively to steps i-iv. Support for the amendment to claim 1 can be found, e.g., in the specification at page 2, line 33 through page 3, line 14, and page 18, first and third paragraphs. New claims 44 and 45 are added herein. Support for new claims 44 and 45 can be found respectively, *e.g.*, in claims 1 and 17 as originally filed. Finally, Applicants have withdrawn claims 7-16, 32-34, 36, and 38-43, which are drawn to non-elected subject matter. No new matter has been added.

Applicants respectfully request that the Examiner reconsider this application in view of the following remarks.

Oath

Applicants acknowledge the Examiner's comments regarding the foreign priority claim described in the oath. A corrected, newly executed oath will be submitted upon receipt of same from Applicants.

Priority

The Examiner has requested a certified copy of the foreign application filed in Denmark on March 7, 2003, to which the present application claims priority. Applicants will submit a certified copy of the foreign application upon receipt of same from the Danish Patent and Trademark Office.

Objection to Drawings

The Examiner has objected to Figure 1 and required the submission of a corrected drawing sheet. *See* the Office Action, page 3. Applicants submit herewith a replacement drawing sheet in compliance with 37 C.F.R. §§ 1.84 and 1.121 to replace Figure 1 as originally filed. No new matter has been added by the replacement drawing presented herein. Applicants request reconsideration and withdrawal of the objection.

Objection to the Specification

The Examiner has objected to the specification as it contains embedded hyperlinks and/or other forms of browser -executable code. *See* the Office Action, page 4. Applicants have amended the specification to delete reference to the objected material. Accordingly, Applicants believe this objection has been overcome.

Sequence Compliance

The Examiner has objected to the specification on the grounds that the specification contains amino acid sequences without corresponding sequence identification numbers and no sequence listing has been submitted. *Id.*

Applicants have amended the specification to include sequence identification numbers for the amino acid sequences disclosed in the specification. Also, Applicants submit herewith a Sequence Listing for those sequences. The Sequence Listing submitted herein is in compliance with the requirements for patent applications containing nucleotide sequences and/or amino acid sequence disclosures. *See* 37 C.F.R. §§ 1.821-1.825. The amendment to the specification and the Sequence Listing in the text file does not include any new matter that goes beyond the disclosure of the as-filed application. Applicants respectfully request the Examiner withdraw the objection.

Rejection under 35 U.S.C. § 112

Claims 1-6, 14-31, 35, and 37 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. *See* the Office Action, pages 4-5.

First, the Examiner has asserted that the phrase "the physicochemical properties" recited in claim 1 lacks sufficient antecedent basis. *Id.*, first paragraph.

Applicants have amended claim 1 to recite "a pseudo-sequence method for identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors, by comparing the physicochemical properties of selected amino acid residues of their binding sites." Amended claim 1 clearly states that the physicochemical properties at issue are those of selected amino acid residues of the binding sites of 7TM receptors. Therefore, the phrase "physicochemical properties" is now clear.

Second, the Examiner has asserted that claim 1 is unclear for reciting two optional steps, i.e., original step i (now deleted) and original step vii (now step iv as recited in amended claim 1). *Id.*, second and third paragraphs. More specifically, the Examiner stands the position that steps ii-v recited in original claim 1 cannot be performed if original step i is not performed.

Applicants disagree. As described in the specification at page 16, second paragraph, and page 18, first paragraph, step i, the alignment step may be omitted, if information about the amino acid residues involved in the 7TM receptor binding sites is already available. As such, steps ii-v recited in original claim 1 can still be performed without performing original step i first. In any event, Applicants have removed original step i from claim 1 without prejudice or disclaimer. The rejection is thus rendered moot.

With respect to the Examiner's request for clarification on the original step vii (now step iv), i.e., the optional ranking step, Applicants confirm that this step is optional and does not have to be performed. There is no absolute need to rank the 7TM receptors to identify a particular receptor which is similar to the first 7TM receptor. For example, the similarity scores obtained in the original step vi (now step iii) can be used in the absence of the optional ranking step.

Finally, the Examiner has asserted that the term "classification" recited in claim 4 as in "a method according to claim 3 wherein the classification is made without using data..." lacks antecedent basis since neither claim 3 nor claim 1, from which claim 3 depends, recite a classification step. *Id.*, fourth paragraph.

Applicants have amended claim 3 to recite a classification step. Support for the amendment can be found in the specification at, e.g., page 8, last paragraph.

In view of the foregoing remarks, Applicants believe that the claims are definite and request that the Examiner reconsider and withdraw the rejection.

Rejection under 35 U.S.C. § 101

Claims 1-6, 14-31, 35, and 37 have been rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter. *See* the Office Action, pages 5-7.

In particular, the Examiner asserts that "a claim to a process or method **must** meet the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (*In re Bilski*, 545F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008))." *Id.*, at page 6; emphasis added. In other words, it is the Examiner's position that the machine-or-transformation

test is the sole test for patentable subject matter. The Examiner then contends that claims 1-6, 14-31, 35, and 37 do not meet the machine-or-transformation test as set forth in *In re Bilski* because "the method steps [recited in these claims] that are critical to the invention are 'not tied to any **particular apparatus** or **machine**' nor do they perform a transformation to a 'different state or thing'...." *Id.*

First, according to *Bilski v. Kappos*, 130 S. Ct. 3218 (2010), "[t]he **machine-or-transformation test is not the sole test** for patent eligibility under § 101. The Court's precedents establish that although that test may be a useful and important clue or investigative tool, it is not the sole test for deciding whether an invention is a patent-eligible 'process' under § 101." *Id.*, at 3221; emphasis added. Therefore, the Examiner erroneously relied on the machine-or-transformation test as the sole test under 35 U.S.C. § 101.

More importantly, the Supreme Court in *Bilksi* emphasized the broad scope of patent eligible subject matter evidenced by the text of 35 U.S.C. § 101 ("any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof") and the intent of Congress that the patent laws be given a wide scope. *Id.*, at 3225.

The claimed methods are not so abstract as to remove them from patent eligibility. The claimed methods are useful for various purposes, including effectively designing compounds having ligands which bind to one or more of target 7TM receptors. The claims address the need for a better technical method to compare various 7TM receptor proteins to produce a result which shows the similarities and differences between binding site structures of the various 7TM receptor proteins. To do so, the claimed methods provide an algorithmic approach to correlating the physicochemical descriptors of selective amino acids of a pseudo-sequence of a 7TM receptor protein with 7TM receptor-ligand interaction features to identify potential ligands and hence design compounds for use in targeted therapy.

Although the claimed methods use mathematical formulas and algorithms, this does not render the methods so abstract as to take them outside of the broad category of patent-eligible processes. The Federal Circuit recognized that algorithms and formulas, even when constituting a significant part of the claimed process, do not necessarily result in a loss of patent eligibility. *Research Corp. v. Microsoft* (Fed. Cir. 2010) Slip Op. at 15. The Federal Circuit also recognized that "inventions with specific applications or improvements to technologies in the marketplace are not likely to be so abstract that they override the statutory language and framework of the

Patent Act." *Id.* Here, rather being directed to an abstract idea or a mathematical formula, the claims are directed to a particular solution to the problem of determining binding site structures to identify potential ligands that can bind to one or more various 7TM receptor proteins and thus design compounds for targeted therapy. Therefore, Applicants submit that the claimed methods fall within the broad statutory category of patent eligible processes. Accordingly, Applicants submit that the claimed subject matter satisfies the requirements of 35 U.S.C. § 101.

Second, Applicants assert that that claims 1-6, 14-31, 35, and 37 nonetheless meet the requirement of the machine-or-transformation test. The claimed methods are directed to identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors, by comparing the physicochemical properties of selected amino acid residues of their binding sites, which reflect 7TM receptor-ligand interaction features. Claims 1-6, 14-31, 35, and 37 require at least the following two steps:

> i) **using a pseudo-sequence** for the first and each of the one or more further 7TM receptor, in which the pseudo-sequence comprises amino acid residues involved in the binding sites or potential binding sites of the first and the one or more further 7TM receptors, **to assign one or more physicochemical descriptors to the amino acid residues of the pseudo-sequence**, wherein the one or more physicochemical descriptors reflect 7TM receptor-ligand interaction features, and
>
> iii) for each of the one or more further 7TM receptor, **generating a similarity score** by comparing the physicochemical descriptor for the first 7TM receptor with the physicochemical descriptors for each of the one or more further 7TM receptors, in which the similarity score quantifies how similar the identified binding sites or potential binding sites of the first 7TM receptor are to those of each of the one or more further 7TM receptors.

Specifically, the active step of "generating a similarity score" to quantify how similar the binding sites of the 7TM receptors are, as required by claims 1-6, 14-31, 35, and 37, transforms the pseudo-sequences of multiple 7TM receptors into a plurality of similarity scores which provide a comparison between binding sites of the multiple 7TM receptors. In addition, these similarity scores are the basis for identification of similarities in binding sites of various 7TM receptors, and hence the active step is critical to the claim methods.

As described above, claims 1-6, 14-31, 35, and 37 meet the transformation requirement of the machine-or-transformation test as the claimed methods include a critical step that transforms the pseudo-sequences of multiple 7TM receptors into a plurality of similarity scores. Furthermore, claim 17 meets the machine requirement of the machine-or-transformation test as the claim requires that the claimed method be tied to a computer having a memory to store the program that executes the claimed method.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. § 102(b)

Claims 1-4, 17, 21-29, and 37 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Lapinsh *et al.*, *Protein Science* 11: 795-805, 2002 ("Lapinsh"). *See* the Office Action, pages 7-8.

As discussed above, claims 1-4, 17, 21-29, and 37 are drawn to methods for identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors. The claimed methods include a step of **using a pseudo-sequence** for the first and each of the one or more further 7TM receptor, in which the pseudo-sequence comprises amino acid residues involved in the binding sites or potential binding sites of the first and the one or more further 7TM receptors, **to assign one or more physicochemical descriptors to the amino acid residues of the pseudo-sequence**, wherein the one or more physicochemical descriptors reflect 7TM receptor-ligand interaction features.

Lapinsh teaches a method for classification of G-protein coupled receptors, by using their primary amino acid sequences. *See* Lapinsh, the title and abstract. Such primary amino acid sequences are distinct from the pseudo-sequence recited in the pending claims. In fact, there is no disclosure in Lapinsh of the use of any pseudo-sequences. Therefore, the instant claims are not anticipated by Lapinsh.

It is noteworthy that Lapinsh merely teaches a method for classifying proteins using their entire amino acid sequences on a phylogenetic basis. *See* Figure 1 on page 797, in which the proteins are separated into phylogenetically-related classes. Although Lapinsh mentions ligand binding class (see the abstract), this is only done on a phylogenetic basis. Accordingly, the Lapinsh method cannot compare ligand binding sites across phylogenetic classes. By contrast,

the claimed methods, by using a pseudo-sequence of the protein sequence for each 7TM receptor, are not constrained by phylogenetic classification. Specifically, this pseudo-sequence can be chosen with knowledge of potential ligand binding sites in mind and because a pseudo-sequence is used rather than a primary amino acid sequence, the claimed methods can be used to identify proteins having similar binding sites but which are classified in different phylogenetic classes.

Further, as discussed above, the claims recite a step of generating a similarity score for each of the one or more further 7TM receptor, by comparing the physicochemical descriptor for the first 7TM receptor with the physicochemical descriptors for each of the one or more further 7TM receptors, in which the similarity score quantifies how similar the identified binding sites or potential binding sites of the first 7TM receptor are to those of each of the one or more further 7TM receptors.

Lapinsh does not expressively or inherently teach such a step. Nor does Lapinsh inherently teach the step recited in these claims. Rather, the Lapinsh method uses an entire primary amino acid sequence for each protein, resulting in excess data noise and hence any binding site similarity would likely be lost in the results.

For the foregoing reasons, the cited method of Lapinsh does not recite each and every element of the present claims and, thus, cannot anticipate the instant invention. Thus, Lapinsh does not teach the claimed invention, either expressly or inherently. As such, Applicants submit this rejection has been overcome and withdrawal is requested.

New claims

New claim 44 depends from claim 1 and new claim 45 requires all the limitations of claim 1. For at least the same reasons set forth above, new claims 44 and 45 are allowable.

CONCLUSION

On the basis of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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